REMARKS

Claims 51, 53, 55-57, 59 and 60 were pending in the application. Claim 57 has been canceled. Claims 51, 53 and 60 have been amended. New claims 61-63 have been added. Accordingly, claims 51, 53, 55, 56 and 59-63 are pending following entry of this amendment.

Support for the amendments to claims 51, 53 and 60 can be found in the claims as originally filed and throughout the specification. Additional support for the amendments to claim 53 can be found in the specification at least at page 30, lines 1-5. Support for new claims 61-63 can be found in the claims as originally filed and throughout the specification. Additional support for new claims 61-63 can be found in the specification at least at page 30, lines 1-5, and at page 47, lines 16-21. No new matter has been added.

Amendments to the claims should in no way be construed as acquiescent to any of the Examiner's rejections and were made solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Claim Rejections Maintained Under 35 USC § 112, First Paragraph

The Examiner has maintained his previous rejection of claims 51, 53 and 55-57 under 35 USC § 112, first paragraph, as lacking written description. The Examiner specifically objects to use of the term "soluble LTβR" as overly broad in view of the species of soluble LTβR defined in the specification. Applicants continue to find this rejection improper for reasons cited in their Amendment filed February 24, 2005. However, solely in the interest of expediting prosecution of the instant application, claim 51 has been amended to specify use of a soluble, human form of LTβR. In the present application, Applicants have functionally characterized a soluble, human form of LTβR, and the specification ***defines the LTβR ligand binding domain as the critical functional domain*** characteristic of any soluble LTβR receptor of the invention. Applicants have further provided a detailed example of a soluble, human form of LTβR as SEQ ID NO:1. One of ordinary skill in the art would understand a soluble, human form of LTβR to include SEQ ID NO:1, as well as functional, ligand-binding fragments of a human LTβR extracellular domain or SEQ ID NO:1,. No additional teaching is necessary for practice of the present invention, as the portion of a human LTβR that is critical for the ligand binding function of the

instant invention is ***the art-recognized ligand binding region contained within the LTβR extracellular domain***. For further proof of the art-recognized nature of the LTβR ligand binding domain, Applicants respectfully direct the Examiner's attention to Figures 4D and 6A of Force *et al.* (*J Immunol.* 155: 5280-5288; referenced within the present specification at least at page 26, lines 14-15). Figure 4D displays the four cysteine-rich repeats of the LTβR ligand binding region that were known at the time of filing to possess functional ligand binding capability. Figure 6A presents detailed sequence information for LTβR, and displays an alignment of LTβR with several other tumor necrosis factor (TNF) family receptors. Cysteine-rich repeats are conserved between all TNF family members, including LTβR, and were definitively identified as critical to ligand binding prior to the time of filing (refer to Banner *et al.* 1993 Cell 73: 431-35, which describes the crystal structure of the TNF receptor-TNF ligand complex). Thus, the molecular topology, sequence and homology information presented in Figures 4D and 6A of the Force *et al.* reference, especially when combined with crystal structure knowledge of TNF receptor family ligand binding domains and the teachings of the present specification, would comprehensively inform one of skill in the art of the scope of the term "soluble, human LTβR" as used in the present specification.

Applicants respectfully remind the Examiner of the recent Federal Circuit holding that where the structure and properties of a protein or domain thereof are known in the art, reanalysis of that protein or domain thereof is not required. *Capon* v. *Dudas* 418 F.3d 1349, 1358 (U.S. App. 2005). The present specification describes a soluble, human form of LTβR to include the LTβR extracellular domain and functional fragments thereof, which are further described as ***those fragments that possess ligand binding activity, an activity that had been ascribed to a specific, art-recognized domain at the time of filing***. Specific guidance regarding the location of ligand binding activity within an LTβR molecule is found at least in Figures 4D and 6A of Force *et al.*, as well as in the crystal structure data of Banner *et al.* The present specification therefore describes the scope of the soluble, human LTβR compositions featured in the instant invention in sufficient detail for one of ordinary skill in the art to recognize the scope of the claimed invention. Applicants therefore request that this rejection be reconsidered and withdrawn.

Claim Rejections Maintained Under Obviousness-Type Double Patenting

The Examiner has additionally maintained his rejection to claims 51, 53 and 55-57 under the judicially-created doctrine of obviousness-type double patenting as being obvious over US Patent 6,403,087 (herein '087) and US Patent 6,669,941 (herein '941). Claim 51 as amended incorporates a limitation consistent with the preamble of said claim into the body of the claim. Specifically, claim 51 is herein amended to specify administration of an effective amount of a soluble lymphotoxin-beta receptor (LTβR) comprising at least one ligand binding domain that can selectively bind to a surface LT ligand fused to one or more heterologous protein domains and a pharmaceutically acceptable carrier, ***such that SLE is treated***. As detailed in Applicants' Amendment of March 10, 2005, the present methods for treatment of SLE are not obvious in view of the '087 and '941 patents, as both patents concern Th1 cell-mediated immune responses. In contrast, SLE is defined in the present application as a systemic autoimmune condition associated with "pathological humoral immune responses". In view of this distinction and the present amendment of claim 51, Applicants request that this rejection be reconsidered and withdrawn. Should the Examiner instead choose to maintain this rejection, while in no way admitting that claims 51, 53 and 55-57 of the present application are obvious over claims 1-14 of the '087 and '941 patents, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate this rejection.

New Claim Rejection Under 35 USC § 112, First Paragraph

The Examiner has newly rejected claims 51, 53 and 55-57 under 35 USC § 112, first paragraph, as lacking the breadth of enablement presently claimed. The foundation for this rejection is the Examiner's objection to use of the term "soluble LTβR" in the present claims. Specifically, the Examiner asserts that "[i]t would require significant study to determine which regions of the extracellular domain or soluble portion of LTβR that is capable of treating SLE, and identifying this portion is in itself an inventive and unpredictable undertaking in itself." The Examiner further cites the fact that "even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein" as reflecting the unpredictability of the art and the state of the prior art. Applicants respectfully traverse this rejection. For reasons cited above and in Applicants' Amendment of March 10, 2005, one of ordinary skill in the art would find the

present specification sufficiently enabling to allow production and use of soluble, human LTβR molecules as covered by the present invention. Within the present specification, Applicants describe the extracellular ligand-binding domain of soluble LTβR as the region of LTβR critical for treatment of SLE. Significant study would therefore not be required to determine which regions of the extracellular domain or soluble portion of LTβR were capable of treating SLE, as Applicants have already identified this portion as the ligand binding domain. Additional support for the art-recognized nature of the LTβR ligand binding domain may be found in the art, at least in Force *et al.* and Banner *et al.*, as described above. Further, the homology data of Force *et al.* and the crystal structure data of Banner *et al.* address the Examiner's contention that the art is unpredictable because even single amino acid substitutions may alter the function of a protein. While the Examiner's statement may hold true for proteins that have not been well-characterized, the domain structure of the extracellular domain of LTβR was well-known at the time of filing, and included, *via* homology, knowledge of the anticipated crystal structure of a LTβR-ligand complex. Specific amino acid residues critical to LTβR ligand binding function were therefore predictable and art-recognized at the time of filing. Thus, the state of the art with respect to the functional domains of soluble, human LTβR was advanced and predictable at the time of filing, and Applicants had described the art-recognized ligand-binding domain of LTβR as a critical domain for use in the compositions featured in the present invention. One of ordinary skill in the art would find the present specification to enable practice of the claimed invention with no more than routine experimentation. Applicants therefore request that this rejection be reconsidered and withdrawn.

New Claim Rejection Under 35 USC § 102

The Examiner has rejected claims 51, 53, 55-57 and 59-60 under 35 USC § 102 as being anticipated by US Patent 5,925,351 (the '351 patent). The Examiner cites *Bristol-Mvers Squibb Company v. Ben Venue Laboratories* against the present application, and states that a manipulative difference in the method steps when compared to the '351 patent does not exist for the present application. 246 F.3d 1368, 1376 (CAFC 2001). This new rejection is improper, as the '351 patent does not teach the administration of the soluble LTβR compounds of the invention as a treatment for SLE. In *Bristol*, all claims considered by the court were directed toward paclitaxel treatment of an identical patient population – a cancer patient population. In contrast, the methods of the present invention require administration of soluble LTβR compounds to an SLE subject/patient population that was not foreseen by the '351 patent. Thus, the present use of soluble LTβR compounds for treatment of SLE was not foreseen by the '351 patent, as the population of subjects treated in the methods of the present invention is distinct and unforeseeable from the subject/patient population described in the '351 patent. Applicants therefore request that this rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. BGNA013CN from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

Amy E. Mandragouras
Registration No.: 36,207
LAHIVE & COCKFIELD, LLP
28 State Street
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant